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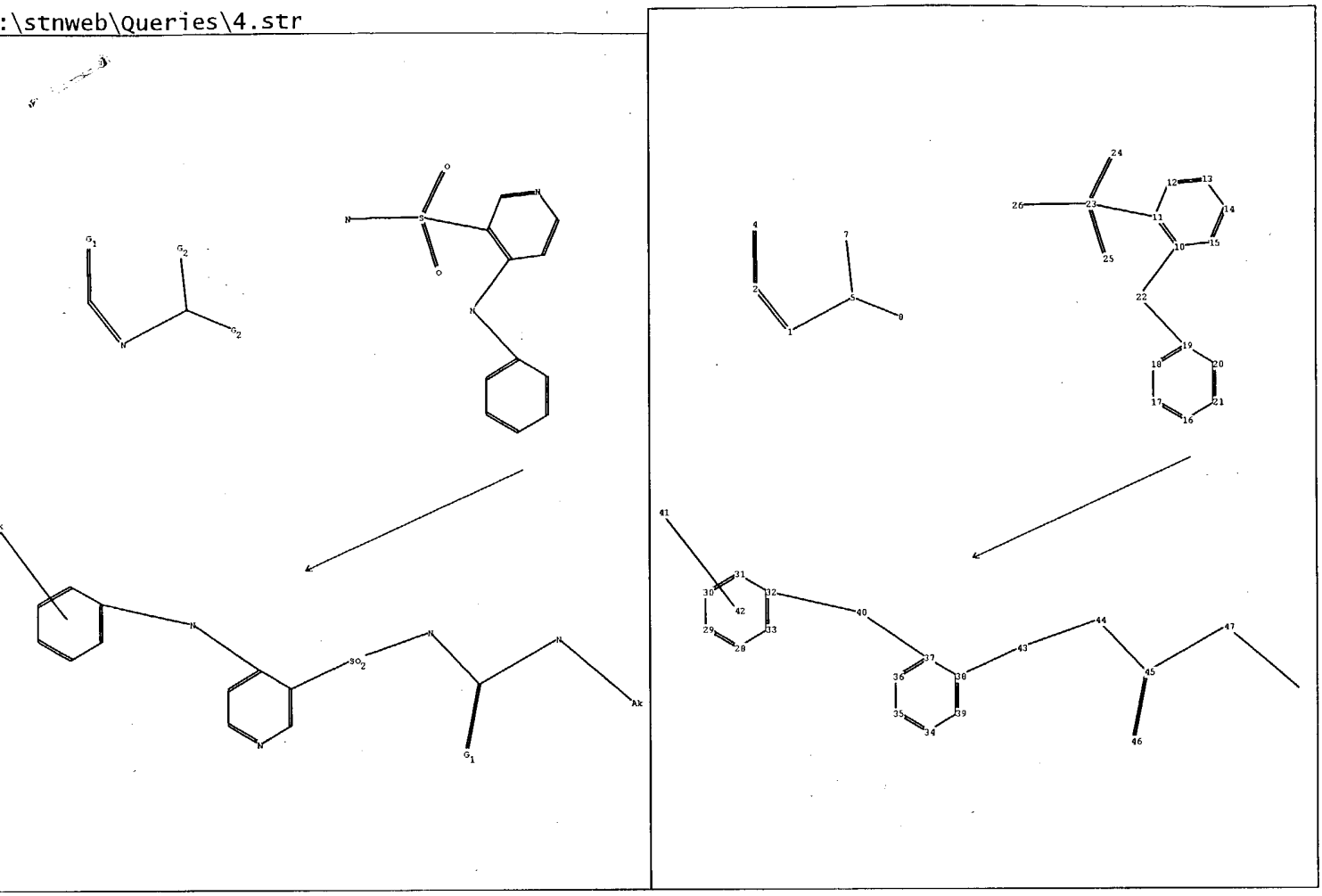


hain nodes :
1 2 4 5 7 8 22 23 24 25 26 40 41 43 44 45 46 47 48
ing nodes :
10 11 12 13 14 15 16 17 18 19 20 21 28 29 30 31 32 33 34 35 36 37
38 39
hain bonds :
1-2 1-5 2-4 5-8 5-7 10-22 11-23 19-22 23-24 23-25 23-26 32-40 37-40 38-43
43-44 44-45 45-46 45-47 47-48
ing bonds :
10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21 17-18 18-19 19-20 20-21 28-29
28-33 29-30 30-31 31-32 32-33 34-35 34-39 35-36 36-37 37-38 38-39
xact/norm bonds :
1-2 1-5 2-4 5-8 5-7 10-22 11-23 19-22 23-24 23-25 23-26 32-40 37-40 43-44
44-45 45-46 45-47 47-48
xact bonds :
38-43
ormalized bonds :
10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21 17-18 18-19 19-20 20-21 28-29
28-33 29-30 30-31 31-32 32-33 34-35 34-39 35-36 36-37 37-38 38-39
solated ring systems :
containing 10 : 16 : 28 : 34 :

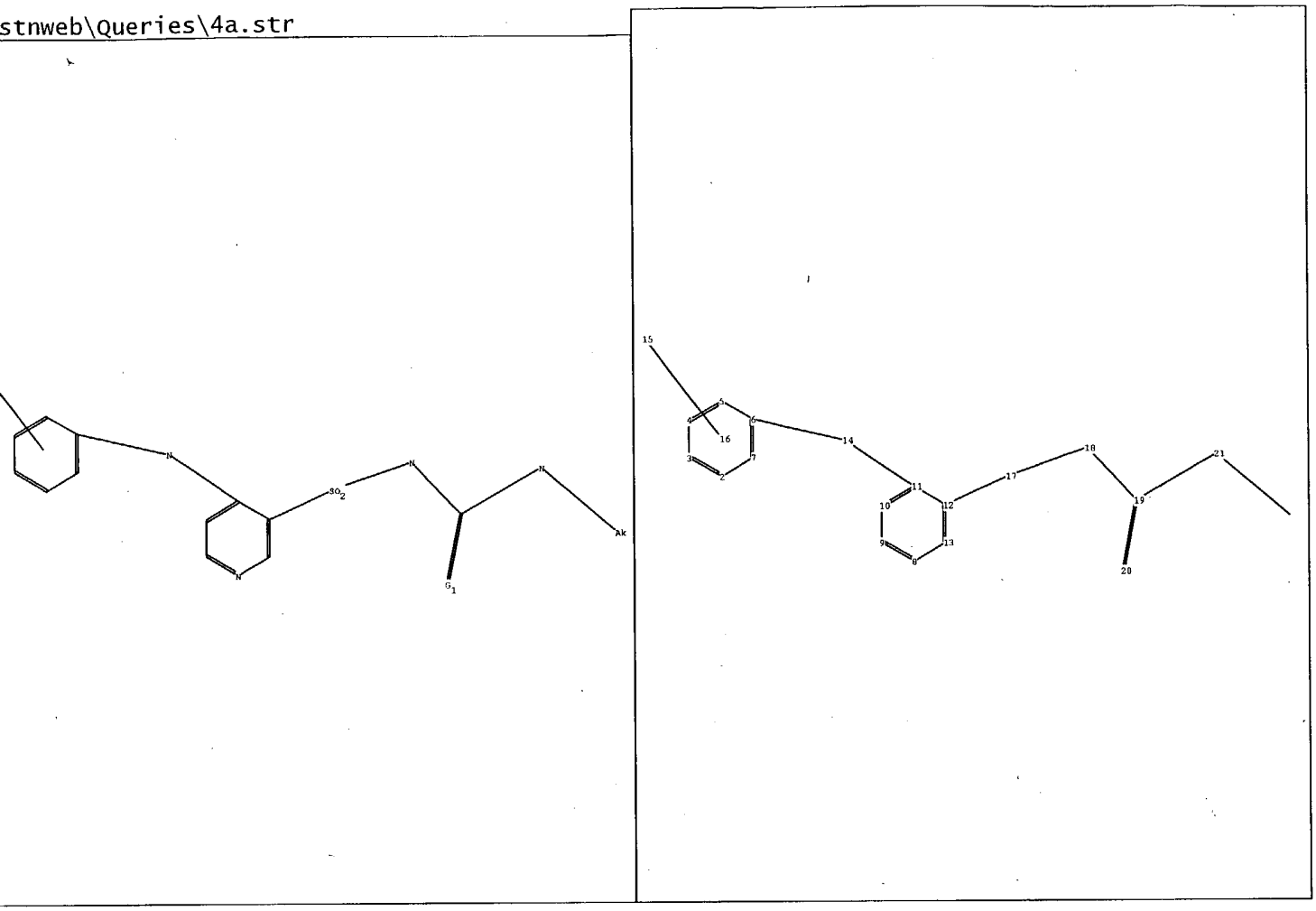
1:O,S

2:CH3,Et

atch level :
1:CLASS 2:CLASS 4:CLASS 5:CLASS 7:CLASS 8:CLASS 10:Atom 11:Atom 12:Atom 13:Atom
14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom 22:CLASS
23:CLASS 24:CLASS 25:CLASS 26:CLASS 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom
33:Atom 34:Atom 35:Atom 36:Atom 37:Atom 38:Atom 39:Atom 40:CLASS 41:CLASS
42:CLASS 43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS
ragments assigned reactant role:

containing 1
containing 10
ragments assigned product role:
containing 28

stnweb\Queries\4a.str



ain nodes :
14 15 17 18 19 20 21 22
ng nodes :
2 3 4 5 6 7 8 9 10 11 12 13
ain bonds :
6-14 11-14 12-17 17-18 18-19 19-20 19-21 21-22
ng bonds :
2-3 2-7 3-4 4-5 5-6 6-7 8-9 8-13 9-10 10-11 11-12 12-13
act/norm bonds :
6-14 11-14 17-18 18-19 19-20 19-21 21-22
act bonds :
12-17
rmalized bonds :
2-3 2-7 3-4 4-5 5-6 6-7 8-9 8-13 9-10 10-11 11-12 12-13

O,S

tch level :
2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom
13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS
22:CLASS

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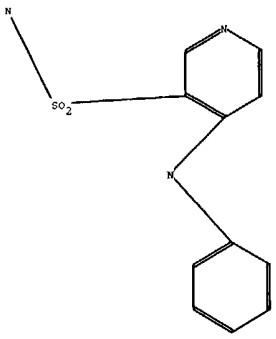
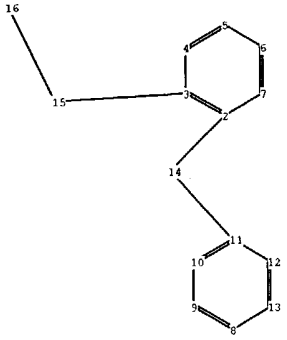


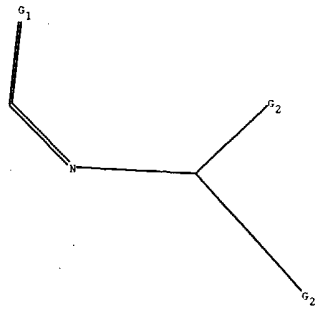


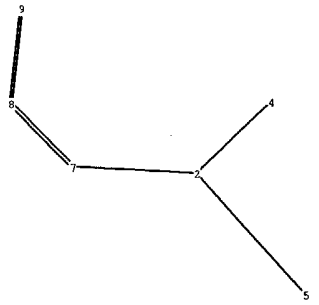
hain nodes :
14 15 16
ing nodes :
2 3 4 5 6 7 8 9 10 11 12 13
hain bonds :
2-14 3-15 11-14 15-16
ing bonds :
2-3 2-7 3-4 4-5 5-6 6-7 8-9 8-13 9-10 10-11 11-12 12-13
xact/norm bonds :
2-14 11-14 15-16
xact bonds :
3-15
ormalized bonds :
2-3 2-7 3-4 4-5 5-6 6-7 8-9 8-13 9-10 10-11 11-12 12-13
solated ring systems :
containing 2 : 8 :

G1:O,S

Match level :
2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom
13:Atom 14:CLASS 15:CLASS 16:CLASS

C:\stnweb\Queries\3a.str





chain nodes :
2 4 5 7 8 9
chain bonds :
2-4 2-5 2-7 7-8 8-9
exact/norm bonds :
2-4 2-5 2-7 7-8 8-9

G1:O,S

G2:CH3,Et

Match level :
2:CLASS 4:CLASS 5:CLASS 7:CLASS 8:CLASS 9:CLASS

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	May 12	EXTEND option available in structure searching
NEWS 4	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS 5	May 27	New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus
NEWS 6	May 27	CAplus super roles and document types searchable in REGISTRY
NEWS 7	Jun 28	Additional enzyme-catalyzed reactions added to CASREACT
NEWS 8	Jun 28	ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG, and WATER from CSA now available on STN(R)
NEWS 9	Jul 12	BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS
NEWS 10	Jul 30	BEILSTEIN on STN workshop to be held August 24 in conjunction with the 228th ACS National Meeting
NEWS 11	AUG 02	IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS 12	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS 13	AUG 02	STN User Update to be held August 22 in conjunction with the 228th ACS National Meeting
NEWS 14	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS 15	AUG 04	Pricing for the Save Answers for SciFinder Wizard within STN Express with Discover! will change September 1, 2004
NEWS 16	AUG 27	BIOCOMMERCE: Changes and enhancements to content coverage
NEWS 17	AUG 27	BIOTECHABS/BIOTECHDS: Two new display fields added for legal status data from INPADOC
NEWS 18	SEP 01	INPADOC: New family current-awareness alert (SDI) available
NEWS 19	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!

NEWS EXPRESS	JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:15:40 ON 01 SEP 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

h eb c g cg b cg eb

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STRUCTURE FILE UPDATES: 31 AUG 2004 HIGHEST RN 736193-62-7
DICTIONARY FILE UPDATES: 31 AUG 2004 HIGHEST RN 736193-62-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> file casreact
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	3.78	3.99

FILE 'CASREACT' ENTERED AT 16:21:07 ON 01 SEP 2004
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26, 1996), unless otherwise indicated in the original publications.

FILE CONTENT:1840 - 29 Aug 2004 VOL 141 ISS 9

****
*
* CASREACT now has more than 8 million reactions *
*
****

Some CASREACT records are derived from the ZIC/VINITI database (1974-1991)
provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
identification.

=>
L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

=> s l1

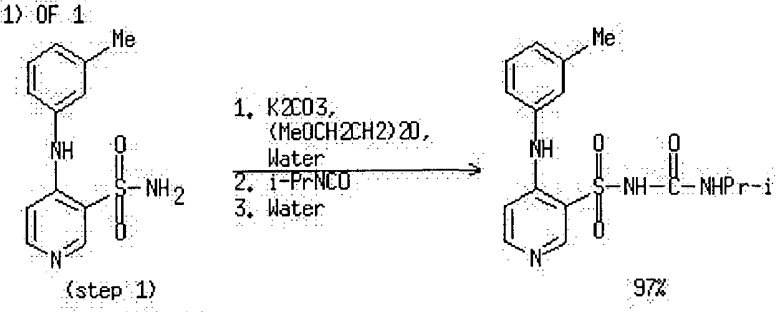
h eb c g cg b cg eb

```
SAMPLE SEARCH INITIATED 16:21:47 FILE 'CASREACT'
SCREENING COMPLETE -      4 REACTIONS TO VERIFY FROM      1 DOCUMENTS

100.0% DONE      4 VERIFIED       1 HIT RXNS                    1 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED VERIFICATIONS:         4 TO      199
PROJECTED ANSWERS:               1 TO       79

L2            1 SEA SSS SAM L1 (     1 REACTIONS)

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'CASREACT' IS 102.30 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:21:51 FILE 'CASREACT'
SCREENING COMPLETE -     11 REACTIONS TO VERIFY FROM      5 DOCUMENTS

100.0% DONE     11 VERIFIED       4 HIT RXNS                    4 DOCS
SEARCH TIME: 00.00.01

L3            4 SEA SSS FUL L1 (     4 REACTIONS)

=> d l3, ibib abs crd, 1-4


L3   ANSWER 1 OF 4  CASREACT  COPYRIGHT 2004 ACS on STN
```

Full Text | CRD References

```
ACCESSION NUMBER:         141:71454  CASREACT
TITLE:                    Process for the preparation of torsemide form II
INVENTOR(S):              Lusanna, Massimiliano; Rainoni, Mauro; Gambuzza,
                          Filippo
PATENT ASSIGNEE(S):       Cosma S.P.A., Italy
SOURCE:                   Eur. Pat. Appl., 28 pp.
                          CODEN: EPXXDW
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     EP 1433784         A1   20040630      EP 2003-29586    20031222
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     US 2004138469      A1   20040715      US 2003-744613   20031222
PRIORITY APPLN. INFO.:                    IT 2002-MI2749   20021223
AB   The present invention relates to a new process for the prepn. of
     torsemide, in particular of pure and stable form II, which comprises
     direct synthesis of torsemide from 4-(3-methylphenylamino)-3-pyridine-
     sulfonamide.  The new process envisages fewer steps than the processes
     described in the prior art, with improved yields and good quality from the
     chem. and preferably polymorphous points of view.
```

RX(1) OF 1



(step 1) 97%

NOTE: optimization study

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

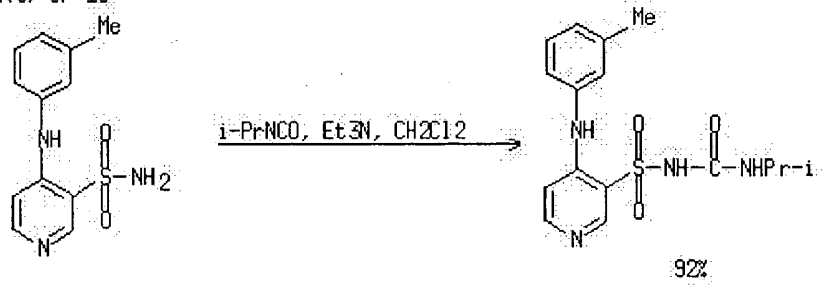
L3 ANSWER 2 OF 4 CASREACT COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 139:197336 CASREACT
TITLE: Synthesis of a new, curative and effective medicine for hypertension and diuretic torasemide
AUTHOR(S): Xiong, Zhenhu; Fei, Xuening
CORPORATE SOURCE: Tianjin Institute of Urban Construction, Tianjin, 300384, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (2002), 12(4), 219-221, 224
CODEN: ZYHZEF; ISSN: 1005-0108
PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Torasemide was prepd. in 5 steps with high yield from 4-hydroxypyridine by sulfonation, chlorination, amidation, substitution with 3-methylaniline, and condensation with iso-Pr isocyanate.

RX(5) OF 15



92%

L3 ANSWER 3 OF 4 CASREACT COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 135:257163 CASREACT
TITLE: Amidation process for preparing 4-chloro-3-pyridinesulfonamide and a method for the preparation of the diuretic torasemide
INVENTOR(S): Kordova, Marco
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

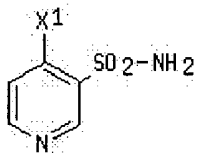
h eb c g cg b cg eb

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070226	A1	20010927	WO 2001-US8866	20010320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002019537	A1	20020214	US 2001-812762	20010320
US 6635765	B2	20031021		
EP 1284733	A1	20030226	EP 2001-920556	20010320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003527425	T2	20030916	JP 2001-568424	20010320
US 2003212277	A1	20031113	US 2003-428463	20030502
US 6670478	B2	20031230		

PRIORITY APPLN. INFO.:
US 2000-190650P 20000320
US 2000-211510P 20000614
US 2001-812762 20010320
WO 2001-US8866 20010320

OTHER SOURCE(S): MARPAT 135:257163
GI



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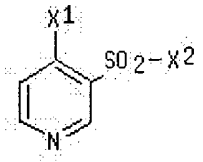
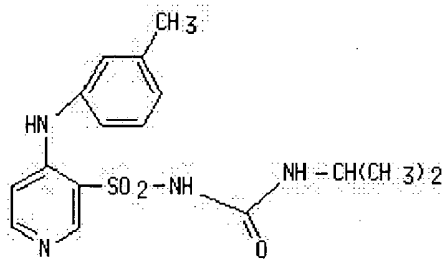


II

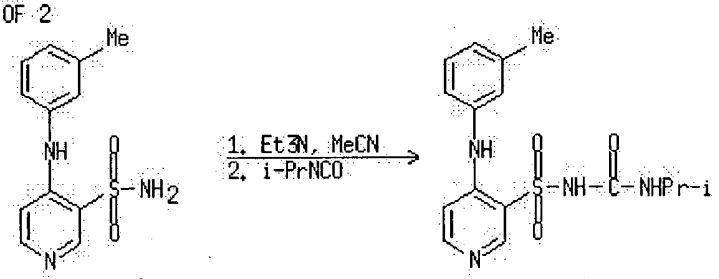


III

AB Torasemide intermediates (I; X1, X2 = Cl, F, Br) are prepd. in high yield and selectivity by the amidation of a halopyridinesulfonyl halide (II) in an org. solvent with ammonia; torasemide (III) is prepd. by the addn. reaction of I (X1 = 3-NHC6H4CH3) in the presence of NEt3 in acetonitrile with iso-Pr isocyanate.

h eb c g cg b cg eb

RX(2) OF 2

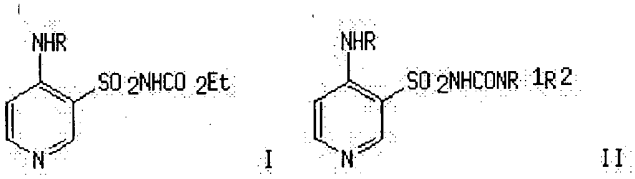


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 CASREACT COPYRIGHT 2004 ACS on STN

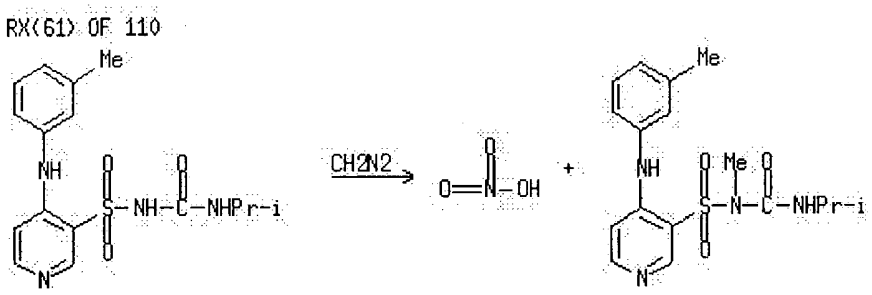
Full Text | Citing References

ACCESSION NUMBER: 94:174826 CASREACT
TITLE: New diuretic torasemide derivatives
AUTHOR(S): Delarge, Jacques; Lapiere, C. L.; De Ridder, Rene; Ghys, Arlette
CORPORATE SOURCE: Lab. Chim. Pharm., Inst. Pharm., Liege, B-4000, Belg.
SOURCE: European Journal of Medicinal Chemistry (1981), 16(1), 65-8
CODEN: EJMCA5; ISSN: 0009-4374
DOCUMENT TYPE: Journal
LANGUAGE: French
GI



AB Carbamates I (R = tolyl, ClC6H4, F3CC6H4, Bu, cyclohexyl, PhCH2CHMe), were treated with amines to yield (pyridinesulfonyl)ureas II [R same as above; R1 = H, alkyl, allyl; R2 = alkyl, allyl, piperidino, morpholino, N-(un)substituted piperidinyl, furfuryl, phenylalkyl, Ph, CH2CH2OH; or NR1R2 = pyrrolidino, morpholino, piperidino, piperazino], which exhibited diuretic activity. I (R = m-tolyl) was heated with CH2:CHCH2NH2 and a mol. sieve in PhMe to give II (R = m-tolyl, R1 = H, R2 = allyl).

RX(61) OF 110



=> file reg

h eb c g cg b cg eb

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   124.30     128.29

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -2.64      -2.64

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STRUCTURE FILE UPDATES:   31 AUG 2004  HIGHEST RN 736193-62-7
DICTIONARY FILE UPDATES:  31 AUG 2004  HIGHEST RN 736193-62-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L4      STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4              STR

=> s l4
SAMPLE SEARCH INITIATED 16:23:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     14 TO ITERATE

100.0% PROCESSED      14 ITERATIONS                          4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           56 TO      504
PROJECTED ANSWERS:               4 TO      200

L5            4 SEA SSS SAM L4

=> s l4 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:23:52 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    235 TO ITERATE

100.0% PROCESSED     235 ITERATIONS                         66 ANSWERS
SEARCH TIME: 00.00.01
```

h eb c g cg b cg eb

```
L6            66 SEA SSS FUL L4

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    156.26     284.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                      0.00      -2.64

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FILE COVERS 1907 - 1 Sep 2004  VOL 141 ISS 10
FILE LAST UPDATED: 31 Aug 2004  (20040831/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> s l5/prep
             3 L5
       3190662 PREP/RL
L7           2 L5/PREP
                 (L5 (L) PREP/RL)

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                      2.36     286.91

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                      0.00      -2.64

FILE 'REGISTRY' ENTERED AT 16:24:04 ON 01 SEP 2004
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   31 AUG 2004  HIGHEST RN 736193-62-7
DICTIONARY FILE UPDATES:  31 AUG 2004  HIGHEST RN 736193-62-7
```

h eb c g cg b cg eb

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

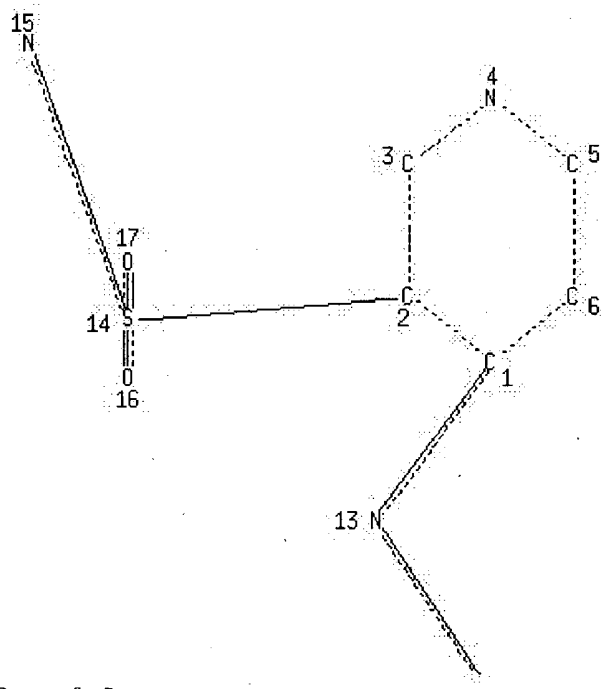
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

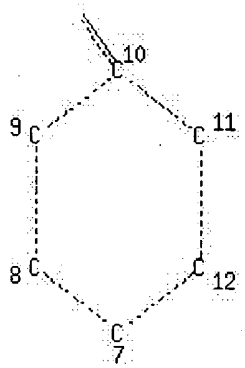
Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L8 STRUCTURE UPLOADED

=> d l8
L8 HAS NO ANSWERS
L8 STR



Page 1-A



Page 2-A
NODE ATTRIBUTES:
NSPEC IS R AT 1
NSPEC IS R AT 2

h eb c g cg b cg eb

```
NSPEC   IS R      AT   3
NSPEC   IS R      AT   4
NSPEC   IS R      AT   5
NSPEC   IS R      AT   6
NSPEC   IS R      AT   7
NSPEC   IS R      AT   8
NSPEC   IS R      AT   9
NSPEC   IS R      AT  10
NSPEC   IS R      AT  11
NSPEC   IS R      AT  12
NSPEC   IS C      AT  13
NSPEC   IS C      AT  14
NSPEC   IS C      AT  15
NSPEC   IS C      AT  16
NSPEC   IS C      AT  17
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  13 14 15 16 17
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  17

STEREO ATTRIBUTES: NONE


=> s l8
SAMPLE SEARCH INITIATED 16:26:19 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     28 TO ITERATE

100.0% PROCESSED      28 ITERATIONS                              12 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:          243 TO      877
PROJECTED ANSWERS:              33 TO      447

L9           12 SEA SSS SAM L8

=> s l8 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:26:23 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     537 TO ITERATE

100.0% PROCESSED     537 ITERATIONS                             259 ANSWERS
SEARCH TIME: 00.00.01

L10          259 SEA SSS FUL L8

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   156.68     443.59

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -2.64
```

h eb c g cg b cg eb

```
FILE 'HCAPLUS' ENTERED AT 16:26:26 ON 01 SEP 2004
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```



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FILE COVERS 1907 - 1 Sep 2004  VOL 141 ISS 10
FILE LAST UPDATED: 31 Aug 2004  (20040831/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> s l10/rct
          309 L10
      2653305 RCT/RL
L11        22 L10/RCT
                (L10 (L) RCT/RL)

=> d his

     (FILE 'HOME' ENTERED AT 16:15:40 ON 01 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 16:15:45 ON 01 SEP 2004

     FILE 'CASREACT' ENTERED AT 16:21:07 ON 01 SEP 2004
L1              STRUCTURE UPLOADED
L2            1 S L1
L3            4 S L1 FULL

     FILE 'REGISTRY' ENTERED AT 16:22:23 ON 01 SEP 2004
L4              STRUCTURE UPLOADED
L5            4 S L4
L6           66 S L4 FULL

     FILE 'HCAPLUS' ENTERED AT 16:23:55 ON 01 SEP 2004
L7            2 S L5/PREP

     FILE 'REGISTRY' ENTERED AT 16:24:04 ON 01 SEP 2004
L8              STRUCTURE UPLOADED
L9           12 S L8
L10         259 S L8 FULL

     FILE 'HCAPLUS' ENTERED AT 16:26:26 ON 01 SEP 2004
L11           22 S L10/RCT

=> s l11 and l7
L12           2 L11 AND L7

=> file reg
```

h eb c g cg b cg eb

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2.36	445.95

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-2.64

FILE 'REGISTRY' ENTERED AT 16:26:37 ON 01 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 31 AUG 2004 HIGHEST RN 736193-62-7
DICTIONARY FILE UPDATES: 31 AUG 2004 HIGHEST RN 736193-62-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

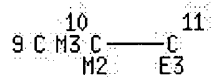
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

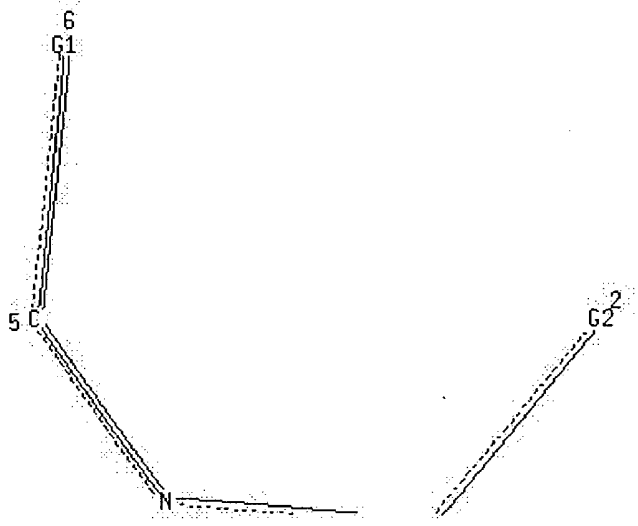
Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L13 STRUCTURE UPLOADED

=> d l13
L13 HAS NO ANSWERS
L13 STR

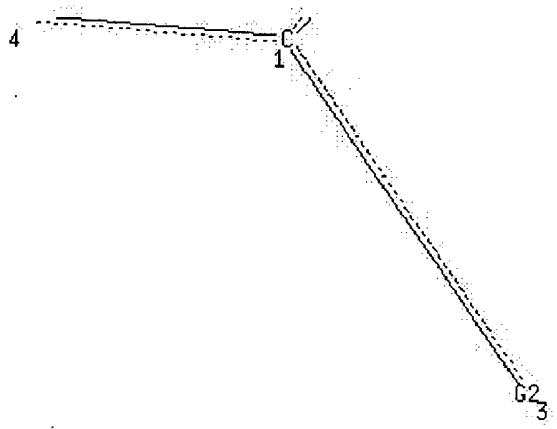


Q 7 S 8
Page 1-A



h eb c g cg b cg eb

Page 1-B



Page 2-B
VAR G1=7/8
VAR G2=9/10
NODE ATTRIBUTES:
HCOUNT IS M3 AT 9
HCOUNT IS M2 AT 10
HCOUNT IS E3 AT 11
NSPEC IS C AT 1
NSPEC IS C AT 2
NSPEC IS C AT 3
NSPEC IS C AT 4
NSPEC IS C AT 5
NSPEC IS C AT 6
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 1 4 5 7 8 9 10 11
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

=> s l13
SAMPLE SEARCH INITIATED 16:28:24 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 247027 TO ITERATE

0.4% PROCESSED 1000 ITERATIONS 20 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **INCOMPLETE**
PROJECTED ITERATIONS: EXCEEDS 1000000
PROJECTED ANSWERS: EXCEEDS 94596

L14 20 SEA SSS SAM L13

=> e isopropyl isocyanate/cn
E1 1 ISOPROPYL ISOBUTYL KETONE/CN
E2 1 ISOPROPYL ISOBUTYRATE/CN
E3 1 --> ISOPROPYL ISOCYANATE/CN
E4 1 ISOPROPYL ISOCYANIDE/CN

h eb c g cg b cg eb

```
E5            1     ISOPROPYL ISOCYANIDE, COMPD. WITH TRIPHENYLBORANE/CN
E6            1     ISOPROPYL ISOCYANIDE, COMPD. WITH TRIPHENYLBORANE (1:1)/CN
E7            1     ISOPROPYL ISOCYANOACETATE/CN
E8            1     ISOPROPYL ISOHEXANOATE/CN
E9            1     ISOPROPYL ISOLAURATE/CN
E10           1     ISOPROPYL ISONITRILE/CN
E11           1     ISOPROPYL ISOPROPANETHIOLSULFINATE/CN
E12           1     ISOPROPYL ISOPROPOXYACETATE/CN

=> s e3
L15           1 "ISOPROPYL ISOCYANATE"/CN

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       6.11     452.06

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00      -2.64

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FILE COVERS 1907 - 1 Sep 2004  VOL 141 ISS 10
FILE LAST UPDATED: 31 Aug 2004  (20040831/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> s l15/rct
          961 L15
      2653305 RCT/RL
L16       838 L15/RCT
                (L15 (L) RCT/RL)

=> d his

     (FILE 'HOME' ENTERED AT 16:15:40 ON 01 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 16:15:45 ON 01 SEP 2004

     FILE 'CASREACT' ENTERED AT 16:21:07 ON 01 SEP 2004
L1              STRUCTURE UPLOADED
L2            1 S L1
L3            4 S L1 FULL
```

h eb c g cg b cg eb

```
     FILE 'REGISTRY' ENTERED AT 16:22:23 ON 01 SEP 2004
L4                STRUCTURE UPLOADED
L5              4 S L4
L6             66 S L4 FULL

     FILE 'HCAPLUS' ENTERED AT 16:23:55 ON 01 SEP 2004
L7              2 S L5/PREP

     FILE 'REGISTRY' ENTERED AT 16:24:04 ON 01 SEP 2004
L8                STRUCTURE UPLOADED
L9             12 S L8
L10           259 S L8 FULL

     FILE 'HCAPLUS' ENTERED AT 16:26:26 ON 01 SEP 2004
L11            22 S L10/RCT
L12             2 S L11 AND L7

     FILE 'REGISTRY' ENTERED AT 16:26:37 ON 01 SEP 2004
L13               STRUCTURE UPLOADED
L14            20 S L13
                  E ISOPROPYL ISOCYANATE/CN
L15             1 S E3

     FILE 'HCAPLUS' ENTERED AT 16:28:55 ON 01 SEP 2004
L16           838 S L15/RCT

=> s l16 and l12
L17             1 L16 AND L12

=> d l17, ibib abs hitstr, 1

L17  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

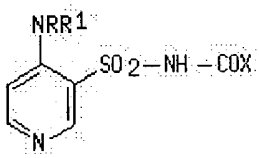
ACCESSION NUMBER: 1980:128730 HCAPLUS
DOCUMENT NUMBER: 92:128730
TITLE: 4-Amino-3-sulfamoylpyridine derivatives and their use
INVENTOR(S): Lapiere, Charles; Delarge, Jacques; Thunus, Leopold; Georges, Andre; De Ridder, Rene; Ghys, Arlette
PATENT ASSIGNEE(S): Christiaens, A., S. A., Belg.
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 3383	A2	19790808	EP 1979-200037	19790122
EP 3383	A3	19790905		
EP 3383	B1	19830209		
R: DE, NL, SE				
GB 1593609	A	19810722	GB 1978-3918	19780131
ES 476658	A1	19790716	ES 1979-476658	19790109
ZA 7900090	A	19801029	ZA 1979-90	19790109
IL 56407	A1	19830515	IL 1979-56407	19790110
AU 7943317	A1	19790809	AU 1979-43317	19790112
AU 524287	B2	19820909		

h eb c g cg b cg eb

CA 1124720	A1	19820601	CA 1979-319934	19790119
BE 873656	A1	19790723	BE 1979-193040	19790123
US 4244950	A	19810113	US 1979-6154	19790124
FR 2416225	A1	19790831	FR 1979-2109	19790126
FR 2416225	B1	19811106		
AT 7900594	A	19840115	AT 1979-594	19790126
AT 375646	B	19840827		
DD 141309	C	19800423	DD 1979-210692	19790129
HU 20570	O	19810828	HU 1979-CI1905	19790130
HU 178203	P	19820328		

PRIORITY APPLN. INFO.: GB 1978-3918 19780131
OTHER SOURCE(S): CASREACT 92:128730
GI

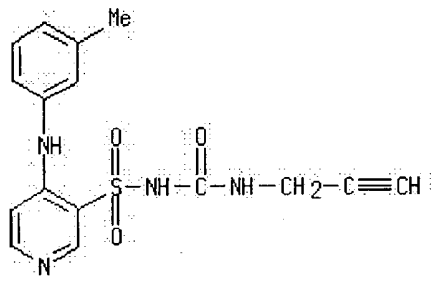


I

AB Diuretic sulfamoylpyridines I [R = H, alkyl, cycloalkyl, R2R3NCO, R2R3NSO2 (R2, R3 = alkyl; R2R3N = heterocyclyl); R1 = alkyl, haloalkyl, cycloalkyl, alkenyl, Ph, phenylalkyl, Ph2CH2, isobornyl, furfuryl, dialkylaminoalkyl; X = substituted amino, alkoxy or heterocyclyl] were prepd. and showed diuretic activity at 25 mg/kg. in mice. Thus, refluxing 3-sulfamido-4-chloropyridine with 3-MeC6H4CH2NH2 in EtOH 9 h gave 3-sulfamido-4-(3-methylbenzyl)aminopyridine, which was treated with Me2CHNCO in CH2Cl2 contg. Et3N 20 h at room temp. to give I (R = H, R1 = 3-MeC6H4CH2, X = Me2CHNH).

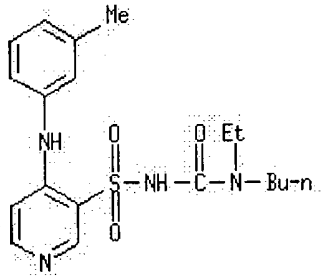
IT **72811-00-8P 72811-63-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(prepn. and diuretic activity of)

RN 72811-00-8 HCAPLUS
CN 3-Pyridinesulfonamide, 4-[(3-methylphenyl)amino]-N-[(2-propynylamino)carbonyl]- (9CI) (CA INDEX NAME)

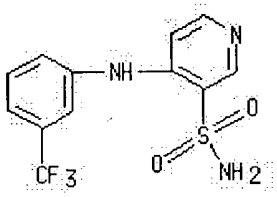


RN 72811-63-3 HCAPLUS
CN 3-Pyridinesulfonamide, N-[(butylethylamino)carbonyl]-4-[(3-methylphenyl)amino]- (9CI) (CA INDEX NAME)

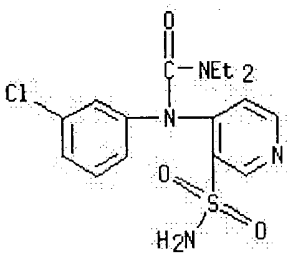
h eb c g cg b cg eb



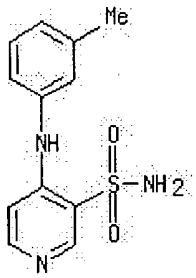
IT 38030-43-2P 72810-58-3P
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with Et isocyanate)
RN 38030-43-2 HCAPLUS
CN 3-Pyridinesulfonamide, 4-[[3-(trifluoromethyl)phenyl]amino]- (9CI) (CA INDEX NAME)



RN 72810-58-3 HCAPLUS
CN 3-Pyridinesulfonamide, 4-[(3-chlorophenyl)[(diethylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)



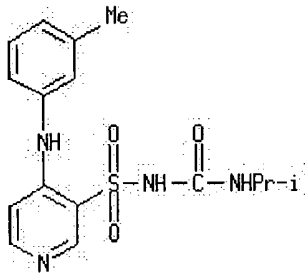
IT 72811-73-5P
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with isopropylisocyanate)
RN 72811-73-5 HCAPLUS
CN 3-Pyridinesulfonamide, 4-[(3-methylphenyl)amino]- (9CI) (CA INDEX NAME)



IT 72810-59-4
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(reaction of, with di-Et carbamoyl chloride)

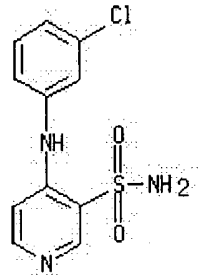
h eb c g cg b cg eb

RN 72810-59-4 HCAPLUS
CN 3-Pyridinesulfonamide, N-[[(1-methylethyl)amino]carbonyl]-4-[(3-methylphenyl)amino]-, sodium salt (9CI) (CA INDEX NAME)

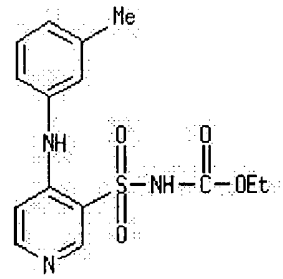


x Na

IT **52214-13-8**
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(reaction of, with diethylcarbamoyl chloride)
RN 52214-13-8 HCAPLUS
CN 3-Pyridinesulfonamide, 4-[(3-chlorophenyl)amino]- (9CI) (CA INDEX NAME)

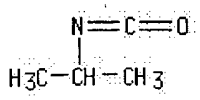


IT **72810-57-2**
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(reaction of, with methylbutylamine)
RN 72810-57-2 HCAPLUS
CN Carbamic acid, [[4-[(3-methylphenyl)amino]-3-pyridinyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)



IT **1795-48-8**
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(reaction of, with sulfamoyl(methylbenzyl)aminopyridine)
RN 1795-48-8 HCAPLUS
CN Propane, 2-isocyanato- (9CI) (CA INDEX NAME)

h eb c g cg b cg eb



RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(reaction of, with sulfamoylaminopyridines

```
=> d his

     (FILE 'HOME' ENTERED AT 16:15:40 ON 01 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 16:15:45 ON 01 SEP 2004

     FILE 'CASREACT' ENTERED AT 16:21:07 ON 01 SEP 2004
L1              STRUCTURE UPLOADED
L2            1 S L1
L3            4 S L1 FULL

     FILE 'REGISTRY' ENTERED AT 16:22:23 ON 01 SEP 2004
L4              STRUCTURE UPLOADED
L5            4 S L4
L6           66 S L4 FULL

     FILE 'HCAPLUS' ENTERED AT 16:23:55 ON 01 SEP 2004
L7            2 S L5/PREP

     FILE 'REGISTRY' ENTERED AT 16:24:04 ON 01 SEP 2004
L8              STRUCTURE UPLOADED
L9           12 S L8
L10         259 S L8 FULL

     FILE 'HCAPLUS' ENTERED AT 16:26:26 ON 01 SEP 2004
L11          22 S L10/RCT
L12           2 S L11 AND L7

     FILE 'REGISTRY' ENTERED AT 16:26:37 ON 01 SEP 2004
L13             STRUCTURE UPLOADED
L14          20 S L13
                E ISOPROPYL ISOCYANATE/CN
L15           1 S E3

     FILE 'HCAPLUS' ENTERED AT 16:28:55 ON 01 SEP 2004
L16         838 S L15/RCT
L17           1 S L16 AND L12

=> s l12 not l17
L18           1 L12 NOT L17

=> d l18, ibib abs hitstr, 1

L18  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
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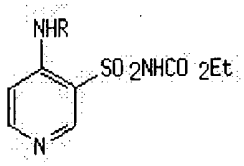
Full Text | More References

```
ACCESSION NUMBER:         1981:174826  HCAPLUS
DOCUMENT NUMBER:          94:174826
TITLE:                    New diuretic torasemide derivatives
AUTHOR(S):                Delarge, Jacques; Lapiere, C. L.; De Ridder, Rene;
                          Ghys, Arlette
CORPORATE SOURCE:         Lab. Chim. Pharm., Inst. Pharm., Liege, B-4000, Belg.
```

h eb c g cg b cg eb

SOURCE: European Journal of Medicinal Chemistry (1981), 16(1), 65-8
CODEN: EJMCA5; ISSN: 0009-4374
DOCUMENT TYPE: Journal
LANGUAGE: French
OTHER SOURCE(S): CASREACT 94:174826
GI



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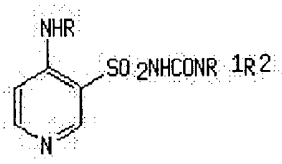
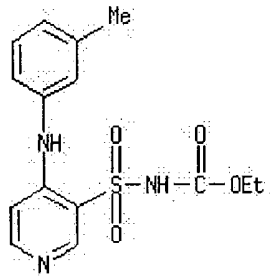


II

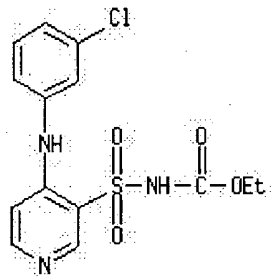
AB Carbamates I (R = tolyl, ClC6H4, F3CC6H4, Bu, cyclohexyl, PhCH2CHMe), were treated with amines to yield (pyridinesulfonyl)ureas II [R same as above; R1 = H, alkyl, allyl; R2 = alkyl, allyl, piperidino, morpholino, N-(un)substituted piperidinyl, furfuryl, phenylalkyl, Ph, CH2CH2OH; or NR1R2 = pyrrolidino, morpholino, piperidino, piperazino], which exhibited diuretic activity. I (R = m-tolyl) was heated with CH2:CHCH2NH2 and a mol. sieve in PhMe to give II (R = m-tolyl, R1 = H, R2 = allyl).

IT **72810-57-2** **72811-25-7** **72811-26-8**
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(amidation of)

RN 72810-57-2 HCAPLUS
CN Carbamic acid, [[4-[(3-methylphenyl)amino]-3-pyridinyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

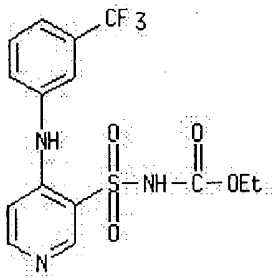


RN 72811-25-7 HCAPLUS
CN Carbamic acid, [[4-[(3-chlorophenyl)amino]-3-pyridinyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

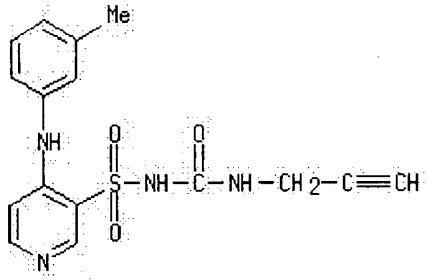


RN 72811-26-8 HCAPLUS
CN Carbamic acid, [[4-[[3-(trifluoromethyl)phenyl]amino]-3-pyridinyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

h eb c g cg b cg eb



IT **72811-00-8P 72811-63-3P 77281-87-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(prepn. and diuretic activity of)
RN 72811-00-8 HCAPLUS
CN 3-Pyridinesulfonamide, 4-[(3-methylphenyl)amino]-N-[(2-propynylamino)carbonyl]- (9CI) (CA INDEX NAME)



RN 72811-63-3 HCAPLUS
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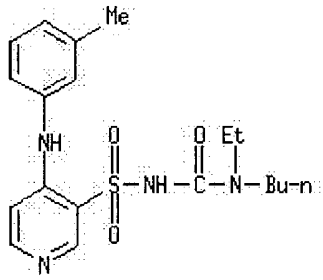

RN 77281-87-9 HCAPLUS
CN 3-Pyridinesulfonamide, 4-[(3-methylphenyl)amino]-N-[[(1-methylpropyl)amino]carbonyl]- (9CI) (CA INDEX NAME)

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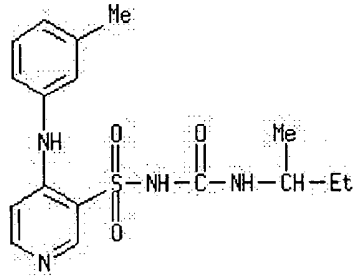
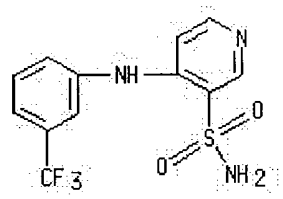


IT 38030-43-2
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(N-mesylation of)
RN 38030-43-2 HCAPLUS
CN 3-Pyridinesulfonamide, 4-[[3-(trifluoromethyl)phenyl]amino]- (9CI) (CA INDEX NAME)



=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	11.88	463.94

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.40	-4.04

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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGistRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d his

(FILE 'HOME' ENTERED AT 16:15:40 ON 01 SEP 2004)

FILE 'REGISTRY' ENTERED AT 16:15:45 ON 01 SEP 2004

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L1                STRUCTURE UPLOADED
L2              1 S L1
L3              4 S L1 FULL

     FILE 'REGISTRY' ENTERED AT 16:22:23 ON 01 SEP 2004
L4                STRUCTURE UPLOADED
L5              4 S L4
L6             66 S L4 FULL

     FILE 'HCAPLUS' ENTERED AT 16:23:55 ON 01 SEP 2004
L7              2 S L5/PREP

     FILE 'REGISTRY' ENTERED AT 16:24:04 ON 01 SEP 2004
L8                STRUCTURE UPLOADED
L9             12 S L8
L10           259 S L8 FULL

     FILE 'HCAPLUS' ENTERED AT 16:26:26 ON 01 SEP 2004
L11            22 S L10/RCT
L12             2 S L11 AND L7

     FILE 'REGISTRY' ENTERED AT 16:26:37 ON 01 SEP 2004
L13               STRUCTURE UPLOADED
L14            20 S L13
                  E ISOPROPYL ISOCYANATE/CN
L15             1 S E3

     FILE 'HCAPLUS' ENTERED AT 16:28:55 ON 01 SEP 2004
L16           838 S L15/RCT
L17             1 S L16 AND L12
L18             1 S L12 NOT L17

     FILE 'CAOLD' ENTERED AT 16:29:39 ON 01 SEP 2004

=> s l6 and l10
                0 L6
                0 L10
L19             0 L6 AND L10

=>
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NEWS 4	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS 5	May 27	New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus
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NEWS 13	AUG 02	STN User Update to be held August 22 in conjunction with the 228th ACS National Meeting
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NEWS 19	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
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=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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FILE COVERS 1907 - 1 Sep 2004 VOL 141 ISS 10
FILE LAST UPDATED: 31 Aug 2004 (20040831/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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=> s torsemide
L1          57 TORSEMIDE

=> s l1 and polymorph?
        155749 POLYMORPH?
L2            8 L1 AND POLYMORPH?

=> s l2 and review/dt
       1754103 REVIEW/DT
L3            2 L2 AND REVIEW/DT

=> d l3, ibib abs, 1-2

L3   ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Cited References

ACCESSION NUMBER: 2000:352882 HCAPLUS
DOCUMENT NUMBER: 133:83770
TITLE: **Torsemide** metabolism by CYP2C9 variants and other human CYP2C subfamily enzymes
AUTHOR(S): Miners, John O.; Coulter, Sally; Birkett, Donald J.; Goldstein, Joyce A.
CORPORATE SOURCE: Department of Clinical Pharmacology, Flinders Medical Centre and Flinders, University School of Medicine, Adelaide, Australia
SOURCE: Pharmacogenetics (2000), 10(3), 267-270
CODEN: PHMCEE; ISSN: 0960-314X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 19 refs. This review describes studies which investigated **torsemide** mthylhydroxylation by the CYP2C9 variants to det. possible effects of CYP2C9 **polymorphism** on **torsemide** elimination in vivo, as well as studies with recombinant CYP 2C8, 2C18 and 2C19 to confirm the isoform selectivity of **torsemide** methylhydroxylation and sulphaphenazole inhibition.

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REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:412144 HCAPLUS
DOCUMENT NUMBER: 129:183680
TITLE: Cytochrome P 450 2C9: an enzyme of major importance in human drug metabolism
AUTHOR(S): Miners, John O.; Birkett, Donald J.
CORPORATE SOURCE: Department of Clinical Pharmacology, Flinders Medical Centre and Flinders University School of Medicine, Bedford Park, SA 5042, Australia
SOURCE: British Journal of Clinical Pharmacology (1998), 45(6), 525-538
CODEN: BCPHBM; ISSN: 0306-5251
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 154 refs. Accumulating evidence indicates that cytochrome P 450 2C9 (CYP2C9) ranks among the most important drug-metabolizing enzymes in humans. Substrates for CYP2C9 include fluoxetine, losartan, phenytoin, tolbutamide, **torsemide**, S-warfarin, and numerous NSAIDs. CYP2C9 activity in vivo is inducible by rifampicin. Evidence suggests that CYP2C9 substrates may also be induced variably by carbamazepine, EtOH, and phenobarbitone. Apart from the mutual competitive inhibition which may occur between alternate substrates, numerous other drugs have been shown to inhibit CYP2C9 activity in vivo and/or in vitro. Clin. significant inhibition may occur with co-administration of amiodarone, fluconazole, phenylbutazone, sulphinpyrazone, sulphaphenazole, and certain other sulfonamides. **Polymorphisms** in the coding region of the CYP2C9 gene produce variants at amino acid residues 144 (R144C) and 359 (I359L) of the CYP2C9 protein. Individuals homozygous for Leu-359 have markedly diminished metabolic capacities for most CYP2C9 substrates, although the frequency of this allele is relatively low. Consistent with the modulation of enzyme activity by genetic and other factors, wide interindividual variability occurs in the elimination and/or dosage requirements of prototypic CYP2C9 substrates. Individualization of dose is essential for those CYP2C9 substrates with a narrow therapeutic index.

REFERENCE COUNT: 154 THERE ARE 154 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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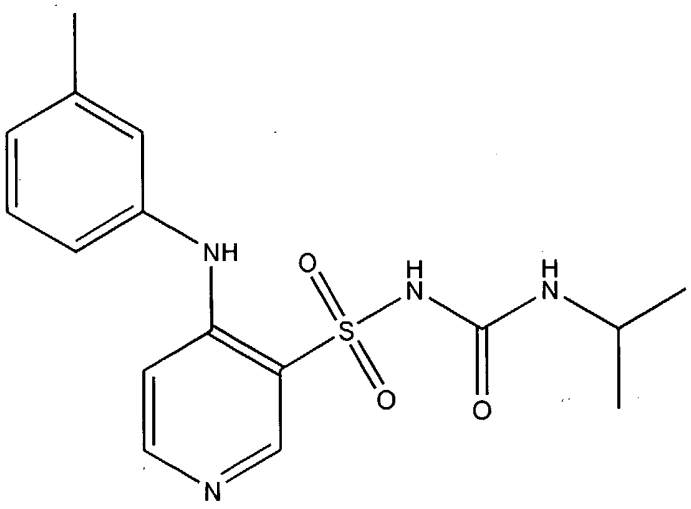
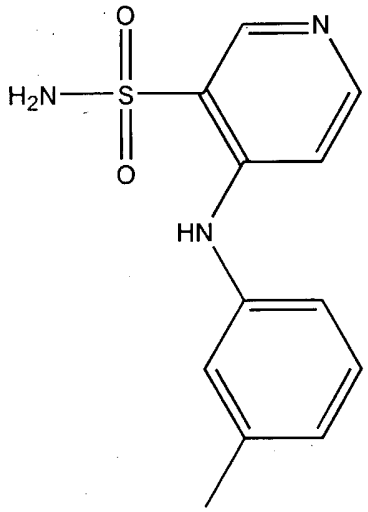


N-[[(1-methylethyl)amino]carbonyl]-4-[(3-methylphenyl)amino]-3-pyridinesulfonamide



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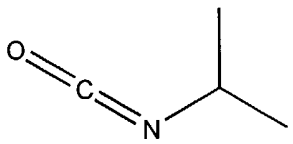

isopropyl isocyanate